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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/089,292	08/28/2002	Hon Mun Ng	8737-000010	9370

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EXAMINER	
LI, BAO Q	

ART UNIT	PAPER NUMBER
1648	

DATE MAILED: 03/10/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/089,292	NG ET AL.	
	Examiner	Art Unit	
	Bao Qun Li	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 July 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-33* is/are pending in the application.

4a) Of the above claim(s) *5-12,18-21 and 26-31* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,13-17,22-25,32 and 33* is/are rejected. claims 24 & 25 can not be allowed due to dependent on rejected claim 22.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The preliminary amendment filed on March 27, 2002 has been acknowledged. Claims 8 12-16, 20, 24 have been amended. Claims 1-33 are pending.

Sequence requirements

This application contains sequence disclosures in Table 9, and line 35 of page 51, and Figs. 1-5 that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason(s) set forth on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures.

Full compliance with the sequence rules is required in response to this Office Action. A complete response to this office action should include both compliance with the sequence rules and a response to the Office Action set forth below. Failure to fully comply with **both** these requirements in the time period set forth in this office action will be held non-responsive.

Election/Restrictions

1. Applicant's election with traverse of Group I, claims 1-4, 13-17, 22-25, 32 and 33 in the reply filed on July 13, 2004 is acknowledged. The traversal is on the ground(s) that US patent No. 5,686,239A (applicants had a typographic error for citing 6,686,239 as 5,686,239) cited in the previous office Action discloses a peptide with 327 amino acids, which is not identical to the present peptide, pE2 having 213 amino acids. Applicants further argue that the claimed peptide is encoded by the carboxy-terminal end of ORF2 (typographic error by Applicants by citing the ORF3 as ORF2), which is only part of ORF2 of HEV and contains conformational antigenic determinations.

2. Applicants' argument has been fully considered. However, This is not found persuasive. Because the scope of elected group I does not limit the claimed peptide to be only 213 amino acid residues and having an conformation epitope. Instead, the claim 1 uses an open language to describe the claimed peptide as any peptide antigen comprising a fragment or analog of pE2 identified as SEQ ID NO: 2. In this context, the polypeptide, SG3 of SEQ ID NO: 13 disclosed

by US patent No. 5,686,239A comprises a fragment of pE2 of SEQ ID NO: 2 with 100% identity. Moreover, Patent "239A" teaches a kit (See claims 1, 2 and 5), and a composition (See lines 47-67 on col. 11) and a method of expressing the antigenic peptide as a recombinant fusion protein fused with glutathione S-transferase (See line 53 of col. 12 through line 1 on col. 13, and example 1 on col. 15-18, especially line 30 on col. 16, lines 41-45 on col. 17). Thus, the cited reference teaches the technical feature of group I. The special technical feature that links all groups of inventions are destroyed.

3. The requirement is still deemed proper and is therefore made FINAL.

4. Claims 1-4, 13-17, 22-25, 32 and 33 are considered before the examiner.

Information Disclosure Statement

5. The information disclosure statement filed on 03/27/2002 fails to comply with 37 CFR 1.98(a)(2), which requires a legible copy of each cited foreign patent document; each non-patent literature publication or that portion which caused it to be listed; and all other information or that portion which caused it to be listed. It has been placed in the application file, but the information referred to therein has not been considered.

6. The information disclosure statement filed 03/27/2003 fails to comply with the provisions of 37 CFR 1.97, 1.98 and MPEP § 609 because lacks of copies of all listed references. It has been placed in the application file, but the information referred to therein has not been considered as to the merits. Applicant is advised that the date of any re-submission of any item of information contained in this information disclosure statement or the submission of any missing element(s) will be the date of submission for purposes of determining compliance with the requirements based on the time of filing the statement, including all certification requirements for statements under 37 CFR 1.97(e). See MPEP § 609 ¶ C(1).

Specification

7. The disclosure is objected to because of the following informalities:

a. The letter "e" is missing in word "determinants" in line 1 of page 32, and the letter "e" is also missing in letter "Determination" of line 1 of Table 6 Title. Appropriate correction is required.

b. There are missing letters in the world of "comparative" in titles of Table 7 and "stool" in the title of Table 8. Appropriate correction is required.

Claim Objections

8. Claim 33 is objected to because of the following informalities: The first letter of claim 33 should be " A" rather than "AN". Appropriate correction is required.

Claim Rejections - 35 USC § 112

9. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

10. Claims 1-4, 13-17, 22-25 and 32-33 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

11. Claims 1 and 22 are vague and indefinite for using a relative term of "similar". Since the specification does not provide a standard for ascertaining the requisite degree of the claimed "similar" and the term of "similar" has many interpretations, one of ordinary skill in the art would not be reasonably determine what the metes and bounds of recited term "similar" are encompassed. Therefore the claim is considered as indefinite. This affects the dependent claims 2-4, 13-17, 23-25 and 32-33.

12. Claim 17 provides for the use of claim 13, but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

Claim Rejections - 35 USC § 101

13. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

14. Claim 17 is rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd.* v. *Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

Claim Rejections - 35 USC § 112

15. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

16. Claims 1-4, 13-17, 23-25 and 32-33.are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter' which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection against the claimed functional fragment or analog or combination thereof and method of using it.

17. In the instant case, the specification only teaches a polypeptide of SEQ ID NO: 2. However, the claims encompass the scope of any or all protein comprising any fragment or analog to any of the aforementioned sequences. Moreover, the claims do not require that the claimed fragment or analog possess any particular distinguished structural feature, or conserved structure. Therefore, the claims are drawn to genus proteins that are not defined by any distinct structure characteristics or sequence identity. However,

18. To provide adequate written description and evidence of possession of a claimed genus protein, the specification must provide sufficient distinguished identifying characteristics of the genus. The factors to be considered include disclosure of, physical and/or chemical properties, functional characteristics, structural/functional correlation, methods of making the claimed

product or any combination thereof. In this case, specification only disclose that the homology sequence is preferred to be at least 80-90% identical (lies 10-13 on page 26. There is no definition about an analog thereof in the specification. There is not even identification of any particular portion of the structure of the sequences that must be conserved for the analog claimed.

19. Vas-Cath. V. Makurkar, 19USPQ2d 111, clearly states "applicant must convey with reasonable clarity to those skilled in the art, as of the filling date sough, he or she was in possession of the invention. The invention is, for purpose of the 'written description' inquiry, whatever is now claimed." (see page 1117). The specification should "clearly allow person of ordinary skill in the art to recognize that [he or she] invented what is claimed.", To be in the possession of any claimed invention, the applicants mush show that a significance of conception and reduction to practice was reached before the application was filed. This concept is further addressed by the court in Fiers v. Sugano where it was emphasized that "[c]onception is a question of law, reviewed de novo on appeal, and if inventor is unable to envision detailed chemical structure of DNA sequence coding for specific protein, as well as method of obtaining it, then conception is not achieved until reduction to practice has occurred, that is, until after gene has been isolated, thus, regardless of complexity or simplicity of method of isolation.

20. While the specification cites that the homology sequence may be at least 80-90% identical to the claimed peptide E2, SEQ ID NO: 2, and to test an immunogenic is well known in the art; applicants do not have any other fragment or analog identified except SEQ ID NO: 2 when the application was filed. Therefore conception of any other protein rather than SEQ ID NO: 2 is not achieved until reduction to practice has occurred regardless of the complexity or simplicity of the method for isolation. Adequate written description requires more than a mere statement of that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. (See Fier v. Revel, 25 USPQ2d 1601 at 1606 (CAFC 1993) and Amgen Inc. v. Chugai Pharmaceutical Co. Ltd., 18 UQPQ2d 1016.

21. Therefore, only isolated protein comprising amino acid sequence of SEQ ID NO: 2, but not any protein comprising any fragment or analog meets the written description provision of 35 U.S.C § 112, first paragraph. Applicant is reminded that Vas-Cath makes clear that the written

description provision of 35 U.S.C § 112 is severable from its enablement provision (See page 1115).

Claim Rejections - 35 USC § 102/103

22. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

23. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

24. Claims 1-4, 13, 22, 23, 24, 25 and 33 are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over by Reyes et al. (US Patent No. 5,686,239A).

25. Claim 1 is drawn to a purified and isolated hepatitis E virus (HEV) antigen peptide, pE2, comprising an amino acid sequence of SEQ ID NO: 2 or homologous sequence fragment or analog thereof having antigen properties similar to the pE2 peptide.

26. Reyes et al. disclose a HEV peptide antigen SG3 of SEQ ID NO: 13, which comprises a carboxyl terminal 327 amino acids of HEV ORF2, and contains 100% identical amino acids of peptide pE2 of SEQ ID NO: 2 except the last three amino acid residues on the C-terminus of pE2. To this context, Reyes et al. disclose a homology sequence fragment or analog of pE2 (See lines 60 on col. 2 through line 4 on col. 3, line 51 on col. 5 and lines 38-48 on col. 7), the claimed is anticipated by the cited reference.

27. Claim 2-4 are directed to the peptide pE2 or fragment or analog thereof is a recombinant fusion protein comprising the heterologous sequence of glutathion S-transferase, and method of making the pE2 peptide or fragment or analog thereof as synthetic or recombinant peptide, wherein the recombinant protein is produced by inserting a nucleic acid sequence encoding the pE2 or fragment or analog thereof into a vector, transformed into a host cell or microorganism capable of expressing the peptide followed by isolation and purification of the peptide or protein.

28. Reyes et al. teach that the peptide antigen SG3 is produced by either a recombination DNA technique (See lines 52-60 on col. 6) or synthetic method (See lines 49-57 on col. 8). The DNA sequence of SEQ ID NO: 7 encodes SG3 that is inserted into a plasmid vector pGEX and transformed into a E Coli host cell. The recombinant Sg3 peptide or protein is then isolated and purified (See lines 57 on col. 17 to lines 67 on col. 18) as a fusion protein fused with glutathion S-transferase by using vector pGEX^{TM}, wherein the pGEX vector is a vector for producing Glutathion S-transferase (GST) fusion protein as evidenced by the catalog of Pharmacia NJ, 1986, pp. 86. Therefore, claims 2-4 are anticipated by the cited reference.

29. Claims 22-23, and 33 are directed to a diagnostic test kit for detecting antibodies to HEV, wherein the kit comprising the purified pE2 or homology sequence, fragment or analog thereof immobilized onto a solid support, an indicator reagent capable of detecting an immunological complex contains the pE2 peptide and other reagents inside the kit including appositive control and antigen diluents.

30. Reyes et al. also disclose that a kit uses the disclosed peptide and method of using the kit foe detecting the presence of the HEV antibody (and claims 5-12). Reyes et al. teach that the kit can be used a solid-phase immune assay for ascertaining the presence of antibodies to HEV in the serum sample taken from HEV susceptive infected patients, wherein the kit comprising a solid support bound with SG3 antigen. While Reye et al. do not teach explicitly the kit comprising a positive control, diluent and/or buffer, but Reye et al. disclose several positive control samples (See Table 4 on col. 17), diluent and buffers routinely used for the HEV ELISA assay (See lines 43-58 on col. 16). Therefore, claims 22 and 33 are anticipated by the disclosure of Reyes. et al.

31. Or alternative, it would have been obvious for a person with ordinary skill in the art to be motivated of using the peptide antigen and other necessary reagents disclosed by Reyes et al. to

make a kit for detecting the presence of HEF antibodies in the serum samples absence unexpected result. Hence the claims 22-23, 24 and 33 as a whole are prima facie obvious absence unexpected results.

Claim Rejections - 35 USC § 102

32. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

33. Claims 1-4, and 13-17 are rejected under 35 U.S.C. 102(b) as being anticipated by Reyes et al. (B) (US patent No. 5,741, 490A) or Reyes et al. (C) (US Patent NO. 5,770,689).

34. Both Reyes et al. (B) and (C) teach an immunogenic composition comprising a HEV antigen polypeptide of HEV ORF2 or C-terminal peptide from HEV ORF2, wherein the polypeptide is SEQ ID NO: 13, 15 or 17, and each of them comprises a fragment that has 100% identity to the claimed pE2 antigen. Reyes et al. also teach a method for making an antibody with disclosed antigen polypeptide or peptide, and a method of using the composition for inducing an immune response to inhibit or prevent the HEV invention in an individual (See Reye (B) & (C) Example 4 on col. 18-19, Example 5 on col. 19, lines 33-63 on col. 10 and REYS et al (B) for claims 1-12). Therefore the claimed invention is anticipated by the cited reference.

Claim Rejections - 35 USC § 102

35. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

36. Claims 1, 4, 32 are rejected under 35 U.S.C. 102(b) as being anticipated by Khudyakov et al. (Virol. 1994, pp. 390-393).

37. Khudyakov et al. disclose several peptide antigens that are all fragments with 100% identical to the amino acid sequence fragment of SEQ ID NO: 2 (See Table 1). All of these peptides except two (No. 30 and No. 38) are antigen determinants as demonstrated by their positive reactions with the anti-HEV positive control sera. Therefore, the claims 1, 4, and 32 are anticipated by the cited reference.

Claim Rejections - 35 USC § 102

38. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

39. Claims 1-4, 13-17, 22 and 33 are rejected under 35 U.S.C. 102(e) as being anticipated by Li et al. (US Patent No. 6,514,690B1).

40. Li et al. disclose a peptide antigen of SEQ ID NO : 18 that comprises a fragment with 100% homology to the claimed peptide E2, wherein the peptide antigen is produced as a glutathion-transferase fusion protein (See examples 1-3, claims 1-14 and examples 7-9). Li et al. teach four antibodies that are generated from the fragment HEV ORF2 that comprise very high homology to the fragment of SEQ ID NO: 2 (See example 12). Li et al. teach a method of making an immunogenic composition comprising the peptide of SEQ ID NO: 18 or fragments of HEV ORF2 or analog thereof that all comprise high homology to the SEQ ID NO: 2 (Example 10). Li et al. also teach a kit for detecting HEV using peptide of SEQ ID NO: 18 or other HEV ORF2 fragment that all have homology to peptide E2, wherein the peptide antigen can be mobilized on to a solid support selected from beads or multi-well microplate, and the detection system utilizes any kind of a reporter molecule (See Claims 15-18 and line 48 on col. 8 through line21 on col. 10). Li et al. also teach to use the peptide of ORF2 as a vaccine to protect the HEV

infection (See Example 10 on col. 19). Therefore the claimed invention is anticipated by the cited reference.

Conclusion

Claims 24-25 are directed to a ELISA plate mobilized with a particular HEV antigen peptide E2, which applicants claim as a special homodimers antigen peptide harboring a conformation epitope due to the frame shift mutation that result in deletion of last three amino acid residues, hereby the pE2 interacts with one another as monomers through dimerization (See lines 20-40 on page 5 and line 1 on page 6 of specification). However, these claims are not allowable because they depend on the rejected claim 22.

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bao Qun Li whose telephone number is 571-272-0904. The examiner can normally be reached on 7:00 am to 3:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on 571-272-0902. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Baoqun Li

Bao Qun Li
03/06/2005